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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,560	07/10/2003	William K. Keener	LIT-PI-529D1	8242

7590 03/18/2005

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EXAMINER	
STUCKER, JEFFREY J	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/618,560	KEENER ET AL.	
	Examiner	Art Unit	
	Jeffrey Stucker	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 7/10/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,627,197. Although the conflicting claims are not identical, they are not patentably distinct from each other because the composition claimed in the patent is not patentably distinct from the composition claimed in the instant method. The instant structure, $(T_m\text{-}A\text{-}X\text{-}B)\text{-}H_n$ or $(A\text{-}X\text{-}B\text{-}T_m)\text{-}H_n$, is the same as the patented structure and has the same or similar constiuents. It would be ovious to use a toxic composition that is activated by a viral enzyme to treat cells infected with the virus encoding the enzyme with the expectation of killing the infected cells, thereby treating the infection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1(ii) is vague and indefinite because it is not clear what a "functional equivalent" of an adenine moiety is. What is the function and how much like an adenine moiety must the equivalent be to fall within the claims?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described

in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one

skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). This rejection is directed to the N-X-A and A-X-N embodiments because there is no teaching in the art or specification as to how this compound will treat HIV because there is no indication that it can specifically target virus or infected cells.

The nature of the invention is therapeutic methods for treating HIV infection comprising administering a compound represented by the formula N-X-A or A-X-N, wherein A is a protein synthesis inactivating protein that is inactive until X is digested, X is a peptide susceptible to digestion by a human immunodeficiency virus protease, and N is an adenine moiety or functional equivalent thereof.

The art is somewhat unpredictable because of the lack of prior art teachings and the lack of working examples in the instant specification.

The quantity of experimentation necessary is extensive even though the relative skill of those in the art is high. There is a great deal of uncertainty in the HIV treatment art. Such factors as the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert

form (cell to cell transmission), as well as via free virus transmission, the existence of latent forms of the virus, the ability of the virus to be shielded in the central nervous system due to the blood-brain barrier, and the complexity and variation of the elaboration of the disease. The existence of these obstacles establish that the contemporary knowledge in the art would not allow one skilled in the art to use the claimed invention with a reasonable expectation of success and without undue experimentation.

As articulated in *In re Marzocchi*: It is incumbent upon the Patent Office, whenever a rejection of this basis is made to explain why it doubts the truth or accuracy of any statement made in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." This standard presupposes that there some statement in the specification concerning the efficacy of the claimed medicinal compound commensurate in scope with the claimed invention. The instant specification only provides some limited statements regarding adenine and pteroic acid inhibiting ricin toxicity. See column 18, lines 1-19.

The state of the prior art is that molecules comprising inactive toxins which are activated by enzymatic

cleavage of an enzyme substrate are known, as excemplified by Borgford, below. However, the molecules comprising the toxin require a means to be attached to a target cell and to move it into the cell where it can be activated by the viral enzyme.

There is no guidance as to how one would use the claimed compositions N-X-A or A-X-N for treating HIV. Further, the instant specification is completely devoid of working examples of using N-X-A or A-X-N for treating any disease, let alone HIV.

The instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. § 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. § 122(b). Therefore, this application is examined under 35 U.S.C. § 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. § 102(e)).

Claims 1-12 are rejected under 35 U.S.C. § 102(a) and (e) as being anticipated by Borgford (6,333,303).

The instant invention is directed to a composition comprising:

$(T_m\text{-}A\text{-}X\text{-}B)\text{-}H_n$ or $(A\text{-}X\text{-}B\text{-}T_m)\text{-}H_n$, or A-X-B wherein

A is a protein synthesis inactivating toxin that is inactive until X is digested,

B is a lectin or a segment thereof,

T is a targeting moiety,

X is a peptide susceptible to digestion by a human immunodeficiency virus protease

H is a hydrophobic agent,

m and n are each 0 or an integer of at least 1.

Borgford teaches a composition comprising ricin A and B chains joined by a linker that is cleaved by HIV protease. See the entire patent. The specifically claimed SEQ ID NO: 12 is disclosed by Borgford as SEQ ID NO: 20. This composition is equivalent to the instantly claimed composition when m and n are each 0.

The reference teaches at column 17, lines 39-49, that the protein of the invention can be conjugated to a cell binding component which could be antibodies to retroviral proteins. The reference goes on to teach how to make the antibodies. This composition is equivalent to the instantly claimed composition when m is 1 and n is 0. The reference teaches that the composition can be prepared in a pharmaceutical composition. See column 19, lines 25-38. Therefore, the instant invention is anticipated by Borgford.

Claims 1-12 are rejected under 35 U.S.C. § 102(b) as being anticipated by Borgford (WO 97/41233).

Borgford teaches a composition comprising ricin A and B chains joined by a linker that is cleaved by HIV protease. See the entire patent. The specifically claimed SEQ ID NO: 12 is disclosed by Borgford as SEQ ID NO: 20. This composition is equivalent to the instantly claimed composition when m and n are

each 0. The reference teaches at page 21, lines 7-14, that the protein of the invention can be conjugated to a cell binding component which could be antibodies to retroviral proteins. The reference goes on to teach how to make the antibodies. This composition is equivalent to the instantly claimed composition when m is 1 and n is 0. The reference teaches that the composition can be prepared in a pharmaceutical composition. See page 23, lines 16-24. Therefore, the instant invention is anticipated by Borgford.

The prior art does not teach or suggest a composition comprising cholic acid or segments the B chain of ricin.

No claims are allowed.

Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

The Group 1600 Official Fax number is: (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on

access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Stucker whose telephone number is (571)-272-0911. The examiner can normally be reached Monday to Thursday from 7:00am-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (571)-272-0902.

JEFFREY STUCKER
PRIMARY EXAMINER